

Amendments to the Specification:

Please replace paragraph [0003] with the following paragraph:

[0003] Mammalian voltage-gated sodium channels are pore-forming membrane proteins responsible for the initiation and propagation of action potentials in excitable membranes in nerve, skeletal muscle and heart cells. The controlled gating of sodium channels in response to membrane depolarizations is necessary for normal electrical signaling and establishing of intercellular communication. Voltage-gated Na⁺ ion channels consist of one large α -subunit (about 200 kDa) and one or two smaller β -subunits. The α -subunits are designated “Nav” (Na for sodium channel and v for voltage-gated), followed by a numbering system for the particular isoform. The Na⁺ channel α -subunit isoforms contain four homologous repeated domains (D1-D4) each with six transmembrane segments (S1-S6). The α -subunit protein alone forms a functional channel when expressed in mammalian expression systems. The four repeated domains are hypothesized to assemble as a ~~pseudotetrameric~~pseudotetrameric structure with the permeation pathway situated at the center. Figure 1 is a cartoon depicting one conceptualization of how the Nav protein arranges itself with respect to the membrane. The cartoon is not accurate; it is an expanded model that does not attempt to depict how the four S6 segments come together to form the sodium channel, but it facilitates an understanding of how the proteins might align with respect to the inside and outside of the excitable membrane. In fact, recent studies suggest that four S6 C-termini may jointly close the voltage-gated cation channel at the cytoplasmic side, probably as an inverted teepee structure.